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| 10/528,848 | 01/23/2006 | Tatsuo Hoshino | 21415 US<br>C038435/0185665 | 2032 |

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| EXAMINER | |
|---|---|
| LONG, SCOTT | |

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| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/528,848 | HOSHINO ET AL. | |
| | Examiner | Art Unit | |
| | Scott D. Long | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,6 and 8-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

*The examiner acknowledges receipt of Claim Amendments and Applicant's Remarks filed on 17 May 2007.*

### *Claim Status*

Claims 1-3 and 6-7 are amended. Claims 4-5 and 7 are cancelled. Claims 9-10 are newly submitted. Claims 1-3, 6, and 8-10 are under current examination.

### *Priority*

This application claims benefit as a 371 of PCT/EP03/10574 (filed 09/23/2003). This application also claims benefit from EUROPEAN PATENT application 02021599.2 (filed 09/27/2002).The instant application has been granted the benefit date, 27 September 2002, from the European application 02021599.2.

### *Response to Arguments - Claim Rejections 35 USC § 112*

*Response to Arguments – 35 USC 112, second paragraph*

Applicant's arguments, see pages 6-20 and Claim amendments, filed 17 May 2007, with respect to claim 6 have been fully considered, but are not persuasive. The previous Action (filed 2/15/2007) stated "claim 6 recited the limitation 'the control

sequences' in line 3 of the claim. There is insufficient antecedent basis for this limitation." Although claim 6 was amended to further limit "the control sequences," there is no reference to "control sequences" earlier in claim 6 or in claim 1. Therefore the examiner maintains that there is no antecedent basis for "the control sequences" in claim 6. Therefore, the rejection of claim 6 under 35 USC 112, second paragraph is hereby maintained.

*Response to Arguments.– 35 USC 112, first paragraph (written description)*

Applicant's arguments (pages 7-8) and Claim amendments, filed 17 May 2007, regarding rejection of claims 2 and 5 have been fully considered and they are found persuasive.

Claim 2 has been amended to remove the phrase, "or a mutant thereof." This amendment satisfactorily obviates the examiner's reasons for rejection. Therefore, the examiner hereby withdraws the rejection of claim 2 under 35 USC 112, first paragraph.

Claim 5 has been cancelled. Therefore, the rejection of claim 5 under 35 USC 112, first paragraph is moot and is hereby withdrawn.

***Response to Arguments - Claim Rejections 35 USC § 103***

Applicant's arguments and claim amendments regarding claims 1-3, 6 and 8 filed 24 November 2006 regarding rejection of claims 1-8 under 35 USC 103 as obvious over Brzostowicz et al. in view of Van Ooyen have been fully considered but they are only partially persuasive.

Claims 4-5 and 7 have been cancelled. Therefore, the rejection of claims 4-5 and 7 under 35 USC 103, is moot and is hereby withdrawn.

The applicant has not argued that the Brzostowicz et al. and Van Ooyen references fail to teach the limitations of claims 1-3, 6 and 8, rather the applicant argues that there is no teaching, suggestion, or motivation in either Brzostowicz et al. or Van Ooyen to reject claims 1-3, 6 and 8 under 35 U.S.C. 103(a) as being unpatentable over Brzostowicz et al. (US Patent 6,969,595, issued 29 November 2005) in view of Van Ooyen (US-5,840,528, issued 24 November 1998). According to the applicant, "there is simply nothing in either of these two documents which discloses or suggests their combination" (page 13, bottom parag.). The examiner suggests that in light of the recent KSR decision, this necessity for a "reason or suggestion" is no longer required. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision Ex parte Smith, --USPQ2d, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396). It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to substitute a known equivalent element for another to obtain predictable results. In the instant case, it would have been obvious to

substitute *Phaffia rhodozyma* as a functionally equivalent microorganism that is useful for production of carotenoids, for any of the microorganisms taught by Brzostowicz et al. Therefore the process as taught by Brzostowicz et al. in view of Van Ooyen would have been prima facie obvious over the method of the instant application.

Therefore, the examiner maintains his rejection of claims 1-3, 6 and 8 under 35 USC 103 as obvious over Brzostowicz et al. in view of Van Ooyen for the reasons of record (Office Action, filed 2/15/2007) and those comments above.

Applicant's arguments and claim amendments regarding claims 1-3, 6 and 8 filed 24 November 2006 regarding rejection of claims 1-8 under 35 USC 103 as obvious over Van Ooyen in view of Cunningham et al. have been fully considered but they are only partially persuasive.

Claims 4-5 and 7 have been cancelled. Therefore, the rejection of claims 4-5 and 7 under 35 USC 103, is moot and is hereby withdrawn.

The applicant has made two different argument against the rejection of claims 1-3, 6 and 8 under 35 USC 103 as obvious over Van Ooyen in view of Cunningham et al. The arguments can be summarized as (1) the references fail to teach all the limitations of the newly amended claims and (2) there is no teaching, suggestion or motivation to combine the references.

The applicant has argued that the Van Ooyen and Cunningham et al. references fail to teach the limitations of claims 1-3, 6 and 8, regarding the newly amended

limitations, "wherein the β –carotene hydroxylase gene is originated from a microorganism which is selected from the group consisting of...Erwinia herbicola" (amended claim 1). Contrary to the applicant's assertion, Cunningham et al. teach E. herbicola β –carotene hydroxylase gene (col.3, line 41 and col.9, lines 11-19).

The applicant also argues that there is no teaching, suggestion, or motivation in either Van Ooyen or Cunningham et al. to reject claims 1-3, 6 and 8 under 35 U.S.C. 103(a) as being unpatentable over Van Ooyen (WO1994/06918, published 31 March 1994) in view of Cunningham et al. (US-5,744,341, issued 28 April 1998). According to the applicant, "there is simply no disclosure or suggestion the cited documents to combine WO1994/06918 and Cunningham in the manner suggested by the Examiner, to arrive at the claimed invention" (page 19, 2nd parag.). The examiner suggests that in light of the recent KSR decision, this necessity for a "reason or suggestion" is no longer required. KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision Ex parte Smith, --USPQ2d, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396). It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to substitute a known equivalent element for another to obtain predictable results. In the instant case, it would have been obvious to substitute any equivalent β –carotene hydroxylase gene, including that of Erwinia herbicola to produce zeaxanthin and β-cryptoxanthin in Phaffia. Therefore the process as taught by Van Ooyen in view of

Cunningham et al. would have been prima facie obvious over the method of the instant application.

Therefore, the examiner maintains his rejection of claims 1-3, 6 and 8 under 35 USC 103 as obvious over Van Ooyen in view of Cunningham et al. for the reasons of record (Office Action, filed 2/15/2007) and those comments above.

## *NEW GROUNDS OF REJECTION*

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention

is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 USC § 112, p 1 "Written Description" Requirement;* (Federal Register/Vol 66. No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claim 3 is broadly drawn, such that it applies to a genus of DNA sequences that are "substantially homologous...more than 90% identical amino acids" to a β-carotene hydroxylase gene of Flavobacterium sp R1534 WT. While the specification (page 3) teaches that the DNA sequences could share a preferable homology of more than 90% similarity to the β-carotene hydroxylase gene and exhibits the same enzymatic activity as the β-carotene hydroxylase gene from *Flavobacterium* R1534 (ATCC21588), the specification fails to detail the necessary structure of the substantially homologous DNA sequences. The nature of which 90% homology is actually important for the claimed enzymatic function has not been described in the specification. In fact, even where the nucleic acid changes have no effect on protein structure or function, these sequences themselves represent allelic variations which have different diagnostic and therapeutic implications.

The Revised Interim Guideline for Examination of Patent Applications under 35 USC § 112, p1 "Written Description" Requirement (Federal Register/ Vol 66. No 4, Friday January 5, 2001) states "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE

ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS", "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (column 2, page 71436, emphasis added).

Appellants are reminded adequate written description requires more than a mere statement that it is a part of the invention and reference to a potential method of isolating or using it. *See Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed Cir. 1991).

*Vas-Cath Inc. v. Mabhurkar*, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, *WHATEVER IS NOW CLAIMED.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize the [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of the above considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed genus of DNA sequences that are "substantially homologous" to a β-carotene hydroxylase gene originated from *Flavobacterium* R1534 (ATCC21588).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brzostowicz et al. (US Patent 6,969,595, issued 29 November 2005) in view of Van Ooyen (US-5,840,528, issued 24 November 1998).

Claim 1 is directed to a process for producing zeaxanthin and β-cryptoxanthin which comprises cultivating a recombinant microorganism which is expresses a β-carotene hydroxylase gene and belongs to the genus *Xanthophyllomyces (Phaffia)* in an aqueous nutrient medium under aerobic conditions, and isolating the resulting carotenoids from the cells of said recombinant microorganism or from the cultured broth, wherein the β-carotene hvdroxylase gene is originated from a microorganism which is selected from the group consisting of *Flavobacterium* SP. R1534 *WT* (ATCC21588). *Erwinia uredovora* ATCCI 932 1 , *Erwinia herbicola* ATCC39368, *Agrobacterium aurantiacum, Alcaliqenes PC-I, Paracoccus marcusii* MH1 , and a gram-negative bacteria E-396 (FERN BP-4283) which have the β-carotene hydroxylase gene and wherein the cultivation is carried out at a pH range from 4 to 8 and at a temperature range from 15 to 26°C for 24 to 500 hours. Brzostowicz et al. teach "a method for the production of a carotenoid compound comprising...[transforming]...at least one isolated nucleic acid molecule encoding an enzyme in the carotenoid biosynthetic pathway under the control of suitable regulatory sequences...under suitable growth conditions...whereby an carotenoid compound is produced" (col 125, lines 44-57). Brzostowicz et al. further teach "the isolated nucleic acid molecule encodes...β-carotene hydroxylase" (col.126, lines 53-57). Brzostowicz et al. also teach, "the carotenoid compound is... β-cryptoxanthin,... zeaxanthin" (col.127, line 39 to col.128,

line 5). Cunningham et al. teach the production of zeaxanthin and β-cryptoxanthin by a microorganism that produces carotenoids and that was transformed with the β –carotene hydroxylase gene from A. thaliana (col.5, lines 35-39; col. 6, lines 37-45). Cunningham et al. also teach E. herbicola β –carotene hydroxylase gene (col.3, line 41 and col.9, lines 11-19). Van Ooyen teaches Phaffia for carotenoid production (page 1, line 22 - page 2, line 29), and suggests that transformation of Phaffia with the crtZ gene can be used for the increased production of carotenoids, e.g. zeaxanthin (page 9, line 36 to page 10, line 6). In addition, the conditions for cultivation of the latter microorganism are disclosed (page 10, lines 30-36; page 11, lines 1-2; pages 12-17; page 21, lines 7-8).

Claim 2 is directed to the process according to claim 1, wherein the recombinant microorganism is derived from *Xanthophyllomyces dendrorhous (Phaffia rhodozyma)* ATCC-9681. Van Ooyen teaches Phaffia for carotenoid production (page 1, line 22 - page 2, line 29), and suggests that transformation of Phaffia with the crtZ gene can be used for the increased production of carotenoids, e.g. zeaxanthin (page 9, line 36 to page 10, line 6).

Claim 3 is directed to the process according to claim 1 or 2, wherein the β-carotene hydroxylase gene is originated from *Flavobacterium* sp. R1534 WT (ATCC21588) or the DNA sequence of the β-carotene hvdroxylase gene is substantially homologous thereto, whereby the amino acid sequence thereof shows more than 90% identical amino acids when compared to the amino acid sequence of crtZ of

line 5). Cunningham et al. teach the production of zeaxanthin and β-cryptoxanthin by a microorganism that produces carotenoids and that was transformed with the β – carotene hydroxylase gene from A. thaliana (col.5, lines 35-39; col. 6, lines 37-45). Cunningham et al. also teach E. herbicola β –carotene hydroxylase gene (col.3, line 41 and col.9, lines 11-19). Van Ooyen teaches Phaffia for carotenoid production (page 1, line 22 - page 2, line 29), and suggests that transformation of Phaffia with the crtZ gene can be used for the increased production of carotenoids, e.g. zeaxanthin (page 9, line 36 to page 10, line 6). In addition, the conditions for cultivation of the latter microorganism are disclosed (page 10, lines 30-36; page 11, lines 1-2; pages 12-17; page 21, lines 7-8).

Claim 2 is directed to the process according to claim 1, wherein the recombinant microorganism is derived from *Xanthophyllomyces dendrorhous (Phaffia rhodozyma)* ATCC-9681. Van Ooyen teaches Phaffia for carotenoid production (page 1, line 22 - page 2, line 29), and suggests that transformation of Phaffia with the crtZ gene can be used for the increased production of carotenoids, e.g. zeaxanthin (page 9, line 36 to page 10, line 6).

Claim 3 is directed to the process according to claim 1 or 2, wherein the β-carotene hydroxylase gene is originated from *Flavobacterium* sp. R1534 WT (ATCC21588) or the DNA sequence of the β-carotene hvdroxylase gene is substantially homologous thereto, whereby the amino acid sequence thereof shows more than 90% identical amino acids when compared to the amino acid sequence of crtZ of

*Flavobacterium* sp. R1534 WT. Brzostowicz et al. teach the β-carotene hydroxylase gene originated from *Flavobacterium* sp. ATCC21588 (col. 25, line 36).

Claim 6 is directed to the process according to claim 1, wherein the a-carotene hydroxylase gene is expressed in the recombinant microorganism using the control sequences, which are capable of effecting the expression of DNA sequences in a microorganism belonging to Phaffia.

Claim 8 is directed to the process according to claim 1,wherein the cultivation is carried out at pH range from 5 to 7 and at a temperature range from 18 to 22°C for 48 to 350 hours. Brzostowicz et al. teach a method for producing zeaxanthin and β-cryptoxanthin, wherein the pH is "maintained constant at 6.95" (col. 57, line 18) and incubation times of 0-69.5 hours (table 15; col. 58, lines 35-45) and at an incubation temperature of 30°C. Van Ooyen teaches that the transformed *Phaffia* "is cultivated under conditions...the range of 15° - 26°C. The preferred range is 20° - 22°C." (col.6, line 24).

Claim 9 is directed to the process according to claim 2, wherein the β-carotene hydroxylase gene is expressed in the recombinant microorganism using the control sequences, which are capable of effecting the expression of DNA sequences in a microorganism belonging to Phaffia. Cunningham teaches vectors comprising promoters (col.6, line 4), suitable for gene expression in Phaffia. Van Ooyen et al teach, "Also disclosed are vectors capable of transforming these strains containing expression regulating sequences active in Phaffia. Preferably, these expression

regulating sequences are obtained from Phaffia. In an exemplified embodiment of the invention the promoter from phaffia is used to regulate expression." (col.2, lines 18-23).

Claim 10 is directed to the process according to claim 3, wherein the β-carotene hydroxylase gene is expressed in the recombinant microorganism using the control sequences, which are capable of effecting the expression of DNA sequences in a microorganism belonging to Phaffia. Cunningham teaches vectors comprising promoters (col.6, line 4), suitable for gene expression in Phaffia. Van Ooyen et al teach, "Also disclosed are vectors capable of transforming these strains containing expression regulating sequences active in Phaffia. Preferably, these expression regulating sequences are obtained from Phaffia. In an exemplified embodiment of the invention the promoter from phaffia is used to regulate expression." (col.2, lines 18-23).

Brzostowicz et al. do not teach the use of genus *Xanthophyllomyces (Phaffia)* as the recombinant microorganism use to express the recombinant proteins.

Van Ooyen teaches transformed *Phaffia rhodozyma* capable of producing carotenoids, including zeaxanthin (col.2, line 50) through introduction of plasmid comprising a suitable gene, "crtZ"(col.5, line 62-63) into *Phaffia rhodozyma*. The applicant will be familiar with the fact that "crtZ" is the name of the gene that encodes β-carotene hydroxylase. Van Ooyen also teaches, "It is possible to produce other carotenoid precursors in the same way, in general all carotenoids that can enzymatically be derived from precursors of astaxanthin in *Phaffia* can be obtained" (col.6, lines 16-19). Van Ooyen teaches Phaffia for carotenoid production (page 1, line 22 - page 2, line 29), and suggests that transformation of Phaffia with the crtZ gene can be used for the

increased production of carotenoids, e.g. zeaxanthin (page 9, line 36 to page 10, line 6). In addition, the conditions for cultivation of the latter microorganism are disclosed (page 10, lines 30-36; page 11, lines 1-2; pages 12-17; page 21, lines 7-8).

Van Ooyen does not teach production of β-cryptoxanthin in Phaffia.

Cunningham et al. teach the production of zeaxanthin and β-cryptoxanthin by a microorganism that produces carotenoids and that was transformed with the β –carotene hydroxylase gene from A. thaliana (col.5, lines 35-39; col. 6, lines 37-45). Cunningham et al. also teach E. herbicola β –carotene hydroxylase gene (col.3, line 41 and col.9, lines 11-19).

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to substitute a known equivalent element for another to obtain predictable results. In the instant case, it would have been obvious to substitute any equivalent β-carotene hydroxylase gene, including that of Erwinia herbicola to produce zeaxanthin and β-cryptoxanthin in Phaffia. Furthermore, it would have been obvious to the person of ordinary skill in the art at the time of the invention was made to substitute a known equivalent element for another to obtain predictable results. In the instant case, it would have been obvious to substitute *Phaffia rhodozyma* as a functionally equivalent microorganism that is useful for production of carotenoids, for any of the microorganisms taught by Brzostowicz et al.

Therefore the process as taught by Brzostowicz et al. in view of Van Ooyen and further in view of Cunningham et al. would have been prima facie obvious over the method of the instant application.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

***Examiner Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott Long
Patent Examiner
Art Unit 1633

*/Janet L. Epps-Ford/*
Primary Examiner
Art Unit 1633

*JLE*